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Supplementary appendix

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Supplement to: McCormack V, McKenzie F, Foerster M, et al. Breast cancer survival and survival gap apportionment in sub-Saharan Africa (ABC-DO): a prospective cohort study. *Lancet Glob Health* 2020; **8**: e1203–12.

Appendix

Supplementary List 1: List of ethics approvals

1. IARC (IEC13-19, IEC15-18)
2. LSHTM (6459)
3. Federal Medical Centre Owerri, Nigeria
4. Abia State University Teaching Hospital, Nigeria
5. University of Zambia Biomedical Research Ethics Committee (004-08-15), Zambia
6. University of Witwatersrand (M150345), Gauteng, South Africa
7. Uganda National Council for Science and Technology (HS 1588), Uganda
8. Ministry of Health and Social Services of Namibia (17/3/3)

Supplementary Information – Statistical methods

We analysed overall survival to three years, on a time-since-diagnosis scale, with this date of diagnosis (“time zero”) defined according to European Network of Cancer Registries guidelines¹ which prioritises date of biopsy, over dates of laboratory receipt, pathology report or first presentation. Follow-up entry date was on the latest of date of diagnosis or ABC-DO recruitment date, and continued to the earliest of date of death, last date alive or administrative censoring on the earliest of 3 years post-diagnosis or 01/01/2019. We examined crude Kaplan-Meier (KM) survival estimates and net survival (stns in STATA), the latter accounting for background age-specific national mortality rates in women for 2015-19, with abridged lifetables smoothed using Ewbank’s 4-parameter model^{2,3}. Age-standardized net survival (ASNS) was calculated using the International Standard Cancer Patient Population-1⁴.

Determinants of survival were examined using Cox’s proportional hazards (stcox) models and flexible parametric survival models (stpm2) using a time-varying baseline hazard with 4 degrees of freedom. The Cox model’s proportional hazard assumption was assessed using the plot of the –cumulative log hazard vs. log survival time, which was significant for stage, hence an interaction was fitted between metastases and time (<6 months, > 6 months) in all models. Because the Cox model does not estimate the baseline hazard needed for predicting survival, and because it does not lend itself easily to the estimation of net survival, we used flexible parametric survival models for these purposes. These more recently developed models model the baseline hazard in a parametric fashion, using a flexible spline function to model the baseline log cumulative hazard, which has been shown to be able to reasonably approximate the baseline hazard (Rutherford et al, J Stat Computation and Simulation, 2013)

A priori prognostic factors examined included age, stage, tumour subtype, treatment and sociodemographic factors using categories specified in Figure 2/Table 2. All models controlled for site-race group using group-specific baseline hazards in Cox models and an indicator variable in flexible parametric models. All hazard ratios were adjusted for age and stage, and model including treatment were additionally adjusted for tumour subtype where known.

Three-year survival was predicted for each site-race group using the following model (STATA command):
stpm2 i.stage07n i.hiv i.educ2 i.agec5 i.gp i.sb i.trt1*meta, bhazard(fitmx) scale(hazard) df(4) iterate(2)

and under the following cumulative scenarios: (i) a stage distribution of 35% stage I/IIA, 25% IIB, 15% IIIA, 10% IIIB, 7% IIIC, 8% stage IV, i.e. an absolute 12% higher stage I/II than the current Sowetan distribution, and where this distribution was already achieved (Namibian non-black), to 60% stage I/IIA, 20% IIB, 5% IIIA, 5% IIIB, 5% IIIC and 5% stage IV. Survival predictions for these stage distributions were made applying the given site+stage’s current treatment distribution. (ii) All women receive systemic therapy+surgery, with treatment effects restricted to that for non-metastatic disease. Thereafter, no survival deficits associated with (iii) HIV-infection; (iv) young age at diagnosis (<30 years); (v) non-ER+/PR+/HER2- tumours; and (vi) reduced education-related deficits, such that each woman was in one category higher (none→primary→secondary→tertiary). In these predictions, the additional mortality associated with lack of combined surgery plus systemic therapy in stage IV women was considered to capture a decision not to treat due to extremely advanced stage IV disease (i.e. a stage effect), not a treatment effect. All analyses were conducted both for all women (n=2120) and, after a Lexis expansion, conditional on surviving to 6-months (1998 women). Sensitivity analyses excluding women with more than 4 months between diagnosis and interview resulted in <2% change in crude survival.

Supplementary Table 1: Previous published estimates of breast cancer survival in sub-Saharan Africa

Region	Country	First author or study (reference)	Ethnicity	Inclusion: Year of diagnosis, race, location	Design, follow-up method	No. breast cancers included (excluded)	Survival specification	1-year survival (%)	2-year survival (%)	3-year survival (%)	5-year survival (%)	Comment regarding inclusions, exclusions and losses to follow-up (LTFU)
East	Ethiopia	Kantelhardt ⁵	Black	2005-10	Prospective, within treatment trial	1070	stage I-III stage I+II, stage III	-	74 85 66		46 72 33	Stage IV excluded. 22% LTFU
East	Ethiopia	Joko-Fru ⁶	Black	Addis Ababa, 2012	PBCR	389	-	91	-	64	-	14% LTFU at 3 y
East	Ethiopia	Eber-Schulz ⁷	Black	2010-16, rural area	Hosp., home visit 2013/16	107	-	78	53	-	-	-
East	Kenya	Joko-Fru ⁶	Black	Nairobi, 2009-13	PBCR	141	-	94	-	76	-	39% LTFU at 3 y
East	Kenya	Joko-Fru ⁶	Black	Eldoret, 2009-13	PBCR	78	-	84	-	50	-	37% LTFU at 3 y
East	Malawi	Msyamboza ⁸	Black	Salima Palliative Care 2006-13	Retrospective	21	-	9.5	0	0	0	Palliative care only
East	Mauritius	Joko-Fru ⁶	Mixed	Mauritius, 2005-09	PBCR	491	-	90	-	78	-	-
East	Mauritius	CONCORD-3 ⁹	Mixed	2005-12	PBCR	483	-	-	-	-	84	-
East	Mauritius	CONCORD-2 ¹⁰	Mixed	2005	PBCR	290	-	-	-	-	87	-
East	Mozambique	Joko-Fru ⁶	Black	Maputo, 2015	PBCR	42	-	76	-	-	-	28% LTFU at 1 y
East	Seychelles	Joko-Fru ⁶	Seychelles	Seychelles, 2008-13	PBCR	105	-	87	-	76	-	1% LTFU at 3 y
East	Uganda	Gakwaya ¹¹	Black	1996-2000, treated women, radiotherapy department	Retrospective review	297	-			-	56	5y survival 74% early / 39% late stage; 26% metastatic
East	Uganda	Galukande ¹²	Black	2004-07 2010-12	Retrospective Hosp.	262	-		94 early stage 56 late stage	-	53	No mention of LTFU.
East	Uganda	SURVCAN ^{13,14}	Black	1993-97 Kampala	PBCR	162	-	75	-	59	44	33% LTFU
East	Uganda	Joko-Fru ⁶	Black	Kyadondo county, 2009-13	PBCR	112	-	74	-	32	-	34% LTFU at 3 y
East	Zimbabwe	Joko-Fru ⁶	Black	Harare, 2009-13	PBCR	174	-	74	-	51	-	1% LTFU at 3 y
East	Zimbabwe	SURVCAN ^{13,15}	Black	1993-97	PBCR	128	-	74	-	55	47	-
East	Zimbabwe	SURVCAN ^{13,15}	White	1993-97	PBCR	116	-	96	-	87	-	-
East	Zimbabwe	Joko-Fru ⁶	Black	Bulawayo, 2012-13	PBCR	54	-	61	-	19	-	41% LTFU at 3 y
East	Zimbabwe	Maguti ¹⁶	Black	1987-90, Mpilo, Bulawayo	Hosp.	25	-	<50	-	-	-	only 25 of 84 followed
Southern	Namibia	Joko-Fru ⁶	Black (majority)	Namibia, 2012-13	PBCR	64	-	95	-	79	-	13% LTFU at 3 y
Southern	S. Africa	Coetzee ¹⁷	NS	2008, public vs. private hospital		240 97	public, private	- -	~80, 94	- -	~65, 92	-
Southern	S. Africa	CONCORD-3 ⁹	Black	2000-14, Eastern Cape	PBCR	733	2000-04, '05-'09, '10-'14	- - -	- - -	- - -	53, 32, 40	-
Southern	S. Africa	Cubasch ¹⁸	majority black	2009-11, Soweto	Hosp. retro	602	stage I/II, stage III/IV	- -	- -	84 56	- -	42% lost at 3 y
Southern	S. Africa	CONCORD-2 ¹⁰	Black	1998-2007, E. Cape	PBCR	372	1995-99	-	-	-	72	-
Southern	S. Africa	Joko-Fru ⁶	Black	Eastern Cape, 2008-13	PBCR	313	-	75		45	-	29% LTFU at 3 y

Southern	S. Africa	Walker ¹⁹	Black	1971-72 and 1980-82 black Soweto	Hosp. retrospective, home visit	113	-	~52	~48	-	-	medians 1.1 and 1.4 y
Southern	S. Africa	CONCORD-2 ¹⁰	Black	1998-2007, E. Cape	PBCR		2000-04, 05-09				38, 53	
West	Benin	Joko-Fru ⁶	Black	Cotonou, 2013-014	PBCR	91		82		53		51% LTFU at 3 y
West	Cote d'Ivoire	Joko-Fru ⁶	Black	Abidjan, 2012-13	PBCR	209		85		51		22% LTFU at 3 y
West	Gambia	SURVCAN ¹³	Black	1993-97	PBCR, active	61	-	30	-	10	10	
West	Gambia	CONCORD-2 ¹⁰	Black	1995-97	PBCR	33	-	-	-	-	12	
West	Ghana	Mensah ²⁰	Black	2002-08 Korle-Bu Teaching hospital	Hosp. retrospective, medical records	1022		~85	~69	~59	48	
West	Ghana	Gyedu ²¹	Black	2013-16	Hosp., biannual call	136		-	69	69	-	
West	Mali	CONCORD-2 ¹⁰	Black	1995-2009 Bamako	PBCR	203	-	-	-	-	14	
West	Mali	CONCORD-3 ⁹	Black	2010-12, Bamako	PBCR	60	-				0	Treated cohort, losses excluded
West	Mali	Joko-Fru ⁶	Black	Bamako, 2012-13	PBCR	48		71		44		23% LTFU at 3 y
West	Mali	Gross Frie ²²	Black	Bamako, 2016	18 month FU call	64	-	~70				
West	Nigeria	Anyanwu ²³	Black	East Noitsha	Hosp. retrospective	78 (46)			~ 60	~45		Median survival 2.6 years, 3.5 y for stage I/II, 1.7 y stage III/IV
West	Nigeria	CONCORD-3 ⁹	Black	2003-14, Ibadan		3962	2005-09, '10-'14				99, 98	
West	Nigeria	Agboola ²⁴	Black	2002-08	Hosp., medical records	255	-			20 to 35		tumour marker study

Hosp. = hospital-based study; NS = not specified ; PBCR=population-based cancer registry

Supplementary Table 2: Characteristics of women recruited into ABC-DO cohort, by recruitment setting and, in Southern Africa, by race

	All	Namibia			South Africa		Uganda	Zambia	Nigeria	Nigeria
Hospitals (capital cities in bold)	NA	Windhoek Central Hospital, AB May Oncology Centre, Windhoek			Chris Hani Baragwanath Academic Hospital, Soweto		Mulago hospital, Uganda Cancer Institute, Kampala	Cancer Diseases Hospital, Lusaka ; Kabwe Hospital	FMC Owerri; ABSUTH§	Maranatha clinic Aba
Catchment population	NA	National (to 1000 km)			Soweto ± 50 km		National (to 600 km)	Provincial and national	Imo and Abia states	Local
Health facility: System level	NA	Tertiary			Tertiary		Tertiary	Sec/Tertiary	Tertiary	NA
Health facility: Sector	NA	Public			Public		Public	Public	Public	Private
Treatment costs to patient	NA	Free/minimal			Low		Out-of-pocket	Out-of-pocket	Out-of-pocket	Out-of-pocket
Treatment availability on site:										
Surgery - endocrine therapy	NA	Yes - Yes			Yes - Yes		Yes - Yes	Yes - Yes	Yes - Yes	Yes - Yes
Chemotherapy – radiotherapy	NA	Yes - Yes			Refer 30 km		Yes - Half time	Yes - Yes	Yes - Referral	Yes - Referral
Recruitment period (month/year)	09/'14-12/'17	09/'14-07/'17			07/'15-12/'17		12/'14-03/'17	01/'16-08/'17	10/'14-04/'17	10/'14-04/'17
Sub-group (race/setting)		White	Mixed race	Black	Black	Mixed race	-	-	Public sector	Private clinic
No. women in ABC-DO cohort	2214	68	37	398	637	36	431	206	321	81
Excluded from survival: No follow-up	7	0	0	0	2	0	0	3	2	0
Breast cancer >2 years prior	51	8	0	14	0	0	10	5	10	5
Cohort for survival analysis	2156	60	37	384†	635	36	421	198	309‡	76
Presenting reason / symptoms										
Breast lump/mass	1378 (94%)	46 (77%)	32 (86)	367 (96%)	NK	NK	387 (93%)	189 (96%)	288 (97%)	69 (92%)
Nipple discharge/retraction	367 (25%)	2 (3%)	5 (14%)	46 (12%)	NK	NK	159 (38%)	32 (16%)	87 (29%)	36 (48%)
Skin redness, dimpling, peau d'orange	312 (51%)	2 (3%)	3 (8%)	23 (6%)	NK	NK	142 (34%)	9 (5%)	95 (32%)	38 (51%)
Abnormal mammogram	97 (1.3%)	29 (48%)	9 (24%)	33 (9%)	NK	NK	22 (5%)	0	3 (1%)	1 (1%)
Fungating/ulcerating tumour	150 (10%)	1 (1.7%)	0	18 (5%)	NK	NK	59 (15\$)	12 (6%)	47 (16%)	13 (17%)
Mean age at diagnosis (SD)	51.8 (14)	59.4 (12)	52.8 (13)	52.7 (15)	55.2 (15)	53.6 (15)	48.3 (13)	49.9 (15)	49.7 (13)	44.8 (9)
% women diagnosed < 40 years	21	3	14	21	15	22	28	28	25	32

Education*: None	305 (15)	0	0	65 (17)	122 (22)	5 (15)	63 (15)	27 (14)	21 (7)	2 (3)
Primary	816 (39)	1 (2)	12 (32)	135 (35)	316 (56)	15 (44)	180 (43)	76 (39)	71 (23)	10 (13)
Secondary	571 (27)	29 (49)	17 (46)	133 (35)	66 (12)	1 (3)	127 (30)	52 (26)	110 (35)	35 (46)
Tertiary	388 (19)	29 (49)	8 (22)	51 (13)	56 (10)	4 (13)	51 (12)	42 (21)	108 (35)	29 (38)
HIV positive N (%)	315 (15)	0	3 (8)	53 (14)	166 (26)	4 (11)	48 (11)	31 (16)	5 (2)	4 (5)
Ever hypertensive N (%)	-	27 (45)	22 (59)	158 (41)	-	-	65 (15)	57 (29)	85 (28)	16 (21)
Obese (BMI> 30 kg/m ²)	466 (22)	27 (45)	19 (51)	120 (31)	48 (8)	6 (17)	69 (16)	63 (32)	83 (27)	31 (41)
Stage at diagnosis: N (%) non-missing	2057 (95)	60 (100)	37 (100)	384 (100)	634 (99)	35 (97)	387 (92)	161 (82)	283 (92)	74 (97)
N (%) 0/I	122 (6)	15 (25)	7 (19)	17 (4)	31 (5)	2 (6)	34 (9)	4 (2)	8 (3)	3 (4)
IIA	325 (16)	19 (32)	7 (19)	56 (16)	130 (21)	10 (29)	60 (16)	15 (9)	23 (8)	5 (7)
IIB	385 (19)	11 (18)	14 (38)	65 (17)	138 (22)	10 (29)	49 (13)	49 (30)	46 (16)	3 (4)
IIIA	336 (16)	4 (7)	2 (5)	88 (23)	95 (15)	5 (14)	59 (15)	18 (11)	54 (19)	11 (15)
IIIB	490 (24)	4 (7)	4 (11)	66 (17)	135 (21)	5 (14)	97 (25)	49 (30)	95 (34)	32 (43)
IIIC	105 (5)	3 (5)	1 (3)	30 (8)	21 (3)	0 (-)	23 (6)	13 (8)	11 (4)	4 (5)
IV	294 (14)	4 (7)	2 (5)	62 (16)	84 (13)	3 (9)	65 (17)	13 (8)	46 (16)	16 (22)
Subtype N known (% known)	1227 (57)	60 (100)	34 (92)	368 (96)	607 (96)	35 (97)	44 (10)	43 (22)	35 (11)	1 (1)
ER+/PR+ HER2-	677 (55)	43 (72)	13 (38)	187 (51)	339 (56)	23 (66)	25 (57)	25 (58)	21 (60)	1 (100)
ER+/PR+ HER2+	257 (21)	8 (13)	8 (24)	84 (23)	139 (23)	8 (23)	3 (7)	4 (9)	3 (9)	0
ER-PR- HER2+	76 (6)	2 (3)	4 (12)	33 (9)	28 (5)	0	5 (11)	3 (7)	1 (3)	0
ER-PR- HER2-	217 (18)	7 (12)	9 (26)	64 (17)	101 (17)	4 (11)	11 (25)	11 (26)	10 (29)	0
Number ER+ (% ER+)	908 (72)	51 (85)	23 (64)	255 (68)	466 (74)	29 (81)	30 (64)	31 (65)	22 (61)	1 (100)
Tumour grade N known (% known)	1398 (65)	52 (87)	30 (81)	282 (73)	602 (95)	36 (100)	251 (60)	103 (52)	38 (12)	4 (5)
Well differentiated	221 (16)	16 (31)	10 (33)	59 (21)	37 (6)	1 (3)	73 (29)	16 (16)	5 (13)	4 (100)
Moderate	671 (48)	21 (40)	13 (43)	138 (49)	317 (53)	22 (61)	78 (31)	53 (51)	29 (76)	0
Poor	506 (36)	15 (29)	7 (23)	85 (30)	248 (41)	13 (36)	100 (40)	34 (33)	4 (11)	0
Treatment: Systemic** and surgery §§	1185 (55)	54 (90)	30 (81)	238 (62)	417 (66)	25 (69)	225 (53)	65 (33)	109 (35)	22 (29)
Systemic** therapy §§	506 (23)	5 (8)	4 (11)	123 (32)	151 (24)	9 (25)	98 (23)	52 (26)	41 (13)	23 (30)
Surgery and/or radiotherapy	122 (6)	1 (2)	3 (8)	19 (5)	16 (3)	2 (6)	25 (6)	8 (4)	41 (13)	7 (9)
None	344 (16)	0	0	4 (1)	51 (8)	0	73 (17)	72 (37)	119 (38)	24 (32)

* n=77 missing; † Of the 384 black women in Namibia, 304 are Namibian, 2 Zimbabwean and 40 Angolan. ‡ 310 Nigerian public sector women include 236 women from Owerri and 74 from Aba. § Federal Medical Centre Owerri and Abia State University Teaching Hospital. §§ with or without radiotherapy. **Systemic therapy includes chemotherapy and/or endocrine therapy.

Supplementary Table 3: Crude survival percentages by site-race group and stage in the ABC-DO cohort.

Survival percentages are only reported if the site-stage category had at least ten women at risk. 100 women without detailed stage information are not included.

Statistic	Site-race group	Breast cancer stage at diagnosis					
		0, I, II a*	II b	III a	III b	III c	IV
No. women all analyses / 6-month analyses	Namibia white	34 / 34	11 / 11	4 / 4	4 / 4	3 / 3	4 / 4
	Namibia MR	14 / 14	14 / 14	2 / 2	4 / 3	1 / 1	2 / 0
	Namibia black	73 / 71	65 / 64	88 / 88	66 / 63	30 / 28	62 / 44
	S. African black	161 / 161	138 / 132	95 / 90	135 / 123	21 / 16	84 / 63
	S. African MR	12 / 12	10 / 10	5 / 5	5 / 4	0 / 0	3 / 3
	Uganda	95 / 94	49 / 46	59 / 58	96 / 92	23 / 19	65 / 40
	Zambia	19 / 19	49 / 43	18 / 18	49 / 39	13 / 6	13 / 4
	Nigeria public	31 / 31	46 / 45	54 / 52	97 / 81	10 / 9	46 / 27
	Nigeria private	8 / 7	3 / 3	11 / 11	32 / 22	4 / 4	16 / 9
	All	447 / 443	385 / 368	336 / 328	490 / 431	105 / 86	294 / 194
No. deaths < 6 + ≥ 6 months	Namibia white	0 + 1	0 + 0	0 + 1	0 + 1	0 + 0	0 + 3
	Namibia MR	0 + 1	0 + 1	0 + 2	1 + 2	0 + 1	2 + 0
	Namibia black	2 + 4	1 + 12	0 + 35	3 + 31	2 + 12	18 + 32
	S. African black	0 + 11	6 + 23	4 + 30	12 + 39	5 + 8	21 + 37
	S. African MR	0 + 2	0 + 0	0 + 0	1 + 2	0 + 0	0 + 2
	Uganda	1 + 30	3 + 11	1 + 21	5 + 51	3 + 11	25 + 32
	Zambia	0 + 5	5 + 6	0 + 8	8 + 13	7 + 1	8 + 2
	Nigeria public	0 + 9	1 + 14	3 + 22	17 + 47	1 + 8	18 + 18
	Nigeria private	1 + 2	0 + 0	0 + 7	10 + 16	0 + 3	7 + 7
	All	4 + 66	16 + 68	7 + 127	57 + 204	18 + 44	99 + 134
Crude 3-year survival (%)	Namibia white	97	100	-	-	-	-
	Namibia MR	93	93	-	-	-	-
	Namibia black	90	75	57	45	49	15
	S. African black	72	71	49	50	26	16
	S. African MR	100	-	-	-	-	-
	Uganda	62	70	59	37	22	7
	Zambia	69	69	51	34	26	30 at 1y
	Nigeria public	63	65	41	22	8	10
	Nigeria private	-	-	26	8	17	2
	All	80	74	51	36	32	12
Crude 3-y survival (%), conditional on being alive at 6 months	Namibia white	97	100	-	-	-	-
	Namibia MR	93	93	-	-	-	-
	Namibia black	94	80	57	48	53	23
	S. African black	92	74	51	55	35	21
	S. African MR	100	-	-	-	-	-
	Uganda	63	75	60	41	27	14
	Zambia	69	79	51	44	-	-
	Nigeria public	63	67	45	27	-	19
	Nigeria private	-	100	26	12	-	-
	All	81	77	53	42	41	20
Crude 6 month survival (%)	Namibia white	100	100	-	-	-	-
	Namibia MR	100	100	-	-	-	-
	Namibia black	96	94	100	94	92	65
	S. African black	100	96	96	91	76	75
	S. African MR	100	-	-	-	-	-
	Uganda	99	93	98	92	81	47
	Zambia	100	88	100	78	32	31
	Nigeria public	100	97	93	79	88	51
	Nigeria private	-	-	100	65	100	44
	All	99	95	97	86	79	59

MR=mixed-race. *

Supplementary Table 4: Therapies received within 12 months of diagnosis, by site (preliminary status if known)

	Namibia	South Africa	Uganda	Zambia	Nigeria
	N (%)	N (%)	N (%)	N (%)	N (%)
Overall treatment combination analysed^a					
None	4 (1)	51 (8)	73 (17)	73 (37)	142 (37)
Surgery only	23 (5)	18 (3)	25 (6)	8 (4)	48 (12)
Systemic therapy, no surgery	132 (27)	160 (24)	98 (23)	52 (26)	64 (17)
Surgery and systemic therapy	322 (67)	442 (66)	225 (53)	65 (33)	131 (34)
Surgery type, if known (1236 (95%) known)					
Mastectomy	298 (91)	410 (89)	200 (90)	63 (98)	92 (57)
Wide local excision	31 (9)	50 (11)	22 (10)	1 (2)	69 (43)
Chemotherapy type					
Neoadjuvant	228 (75)	63% ^d	24 (39)	73 (76)	74 (80)
Adjuvant	76 (25)	37% ^d	38 (61)	23 (24)	19 (20)
First chemotherapy regimen ^b					
CAF	69 (23)	33 (8)	48 (77)	40 (42)	58 (62)
CAFT	79 (26)	11 (3)	-	-	-
CAT	11 (4)	252 (63)	6 (10)	43 (45)	6 (6)
CA	49 (16)	52 (16)	7 (11)	1 (1)	21 (23)
CMF	3 (1)	11 (3)	1 (2)	8 (8)	1 (1)
Taxane only	10 (3)	23 (6)	-	3 (3)	6 (6)
Xeloda	2 (1)	2 (<1)	-	-	-
CA-T	81 (27)	-	-	-	1 (1)
Other	-	4 (1)	-	1 (1)	-
Total N if known	<u>304</u>	<u>398</u>	<u>62</u>	<u>96</u>	<u>93</u>
Radiotherapy received	Yes		71 (17)	29 (15)	12 (3)
Endocrine therapy ^c	Yes		66 (16)	41 (21)	94 (24)

^aTreatment combinations did not include radiotherapy.

^bChemotherapy drugs: CAF = Cyclophosphamide + anthracycline (Adriamycin (doxorubicin)/epirubicin) + Fluoracil; CAFT = CAF + taxane; CAT = Cyclophosphamide + anthracycline + taxane; CA Cyclophosphamide + anthracycline; CMF = cyclophosphamide + methotrexate + Fluorouracil; CA-T: Cyclophosphamide + anthracycline followed by taxane;

^cEndocrine therapy is predominantly tamoxifen at each site, and includes aromatase inhibitors (9% in Namibia, 8% Zambia), Herceptin (5% Namibia) and ovarian ablation (3% Namibia).

^dClinic-level data from O'Neil DS et al, The Oncologist, 2019, 24:933-944

Supplementary Table 5: Hazard ratios (HR) of death from all causes in the ABC-DO cohort in relation to type of treatment received, by site and stage

Stage	Treatment	All		Namibia		Uganda		Zambia		Nigeria		South Africa	
		No. deaths / women	HR (95% CI)	No. deaths / women	HR (95% CI)	No. deaths / women	HR (95% CI)	No. deaths / women	HR (95% CI)	No. deaths / women	HR (95% CI)	No. deaths / women	HR (95% CI)
Stage 0/I/II	None	29/85	2.1 (1.3, 3.4)	2 / 2	-	10/24	2.9 (1.3, 6.4)	7/19	3.9 (1.1, 13.3)	8/25	0.9 (0.3, 2.3)	1 / 14	0.6 (0.1, 4.1)
	Surgery only	13/56	1.2 (0.7, 2.3)	0/5	-	3/9	1.5 (0.4, 5.6)	0 / 4	-	6/24	0.7 (0.2, 1.9)	4 / 14	2.6 (0.9, 7.4)
	Systemic only	28/89	2.3 (1.4, 3.5)	5 / 28	0.9 (0.3, 2.8)	13/21	4.6 (2.2, 9.7)	4/15	2.1 (0.5, 8.1)	1/3	-	5 / 22	1.9 (0.7, 5.0)
	Surgery + systemic	82/601	1	14/174	1	19/90	1	5/30	1	12/36	1	32 / 271	1
Stage III	None	93/141	2.4 (1.8, 3.2)	0/0	-	14/22	2.4 (1.3, 4.6)	16/26	5.3 (1.8, 15.8)	49 / 71	1.9 (1.2, 2.9)	13 / 21	4.9 (2.5, 9.5)
	Surgery only	19/33	1.5 (0.9, 2.4)	0/0	-	5/9	1.6 (0.6, 4.0)	1/2	-	11/18	1.3 (0.7, 2.5)	2/4	-
	Systemic only	161/269	2.0 (1.6, 2.6)	38/66	2.2 (1.4, 3.6)	34/51	1.8 (1.1, 2.9)	12/30	2.0 (0.7, 6.0)	32 / 42	2.0 (1.2, 3.3)	45 / 80	3.2 (2.1, 5.1)
	Surgery + systemic	178/478	1	47/127	1	39/96	1	8/22	1	42 / 77	1	41 / 156	1
Stage IV	None	60/62	4.6 (3.0, 7.1)	2/2	-	13/13	86.0(2.4, 14.6)	4/4	-	27 / 28	3.5 (1.3, 9.3)	14 / 15	7.5 (2.9,19.6)
	Surgery only	4/7	-	1/1	-	1/1	-	3/5	-	2/5	-	0 / 0	-
	Systemic only	108/140	1.9 (1.3, 2.7)	31/38	1.5 (0.8, 3.0)	22/23	6.2 (0.7, 54.0)	2/3	-	14 / 17	1.6 (0.6, 4.4)	38 / 57	2.2 (1.0, 5.2)
	Surgery + systemic	54/78	1	15/21	1	21/28	1	1/1	-	8/11	1	8/15	1

HRs estimated via Cox proportional hazards models. Systemic therapy includes chemotherapy and/or endocrine therapy. For each site, HRs only reported if there were at least 10 women with that treatment combination. HRs are adjusted for age at diagnosis (<30, 30 to <40, 40 to <50, 50 to <60, 60 to <70, 70+ years), sub-categories within each stage category (I/IIA, IIB, IIIA, IIIB, IIIC and IV where appropriate), subtype (ER+/PR+HER2-, ER+/PR+HER2+, ER-PR-HER2+, ER-PR-HER2- where known), and the baseline hazard is stratified by race in Southern Africa and by site-race group for all-site analyses. Nigerian analyses include a separate baseline hazard for the 3 hospitals. CI = confidence interval; HR

Supplementary Table 6: Hazard ratios (HR) of death from all causes in relation to treatment received, by time since diagnosis and stage

		All	All sites, within 6 months			All sites, beyond 6 months	
	Treatment	No. deaths / women	HR (95% CI)	No. deaths / women	HR (95% CI)	No. deaths / women	HR (95% CI)
Stage 0/I/II	None	29 / 85	2.1 (1.3, 3.3)	8 / 80	10.9 (2.8, 43.4)	21 / 77	1.6 (1.0, 2.7)
	Surgery only	13 / 56	1.2 (0.6, 2.2)	0 / 55	<0.1	13 / 56	1.2 (0.6, 2.2)
	Systemic, no sx	28 / 89	2.2 (1.4, 3.5)	8 / 86	9.3 (2.6, 33.0)	20 / 80	1.8 (1.1, 3.0)
	Systemic + sx	83 / 600	1	4 / 576	1	79 / 596	1
Stage III	None	93 / 141	2.4 (1.8, 3.2)	39 / 135	9.7 (4.5, 21.1)	54 / 102	1.7 (1.2, 2.4)
	Surgery only	19 / 33	1.5 (0.9, 2.5)	0 / 32	<0.1	19 / 33	1.6 (1.0, 2.7)
	Systemic, no sx	161 / 269	2.1 (1.6, 2.6)	33 / 252	4.8 (2.2, 10.1)	128 / 232	1.9 (1.5, 2.5)
	Systemic + sx	178 / 479	1	9 / 448	1	169 / 470	1
Stage IV	None	60 / 62	4.6 (3.0, 7.1)	43 / 60	10.1 (4.6, 22.5)	17 / 19	2.6 (1.4, 4.8)
	Surgery only	4 / 7	-	1 / 7	-	3 / 6	-
	Systemic, no sx	108 / 140	1.9 (1.3, 2.7)	43 / 131	3.4 (1.6, 7.4)	66 / 96	1.5 (1.0, 2.3)
	Systemic + sx	54 / 78	1	8 / 67	1	46 / 70	1

Sx = breast surgery; HRs estimated via Cox proportional hazards. For each site, HRs only reported if there were at least 10 women with that treatment combination. HRs are adjusted for age (5-years categories), sub-divisions of stage within each stage category (I/IIA, IIB, IIIA, IIIB, IIIC and IV where appropriate), and the baseline hazard is stratified by race in Namibia and South Africa and by site-race group for all-site analyses. B Nigerian analyses include a separate baseline hazard for the public and private sector.

Supplementary Table 7: Hazards ratios (HR) for death from all causes after breast cancer diagnosis in the ABC-DO cohort. Mutually adjusted hazard ratios estimated from flexible proportional survival models for overall survival to 3-years for all women and for those alive at 6-months post diagnosis. All models are restricted to public hospital settings. Hazards ratios in bold are significant at the 5% level.

		Overall survival to 3 years		Overall survival to 3 years if alive at 6-months	
No. deaths / women		812 / 2063		619 / 1863	
		No. deaths	HR (95% CI)	No. deaths	HR (95% CI)
Stage	0/I/IIA	67	1	64	
	IIB	83	1.77 (1.20, 2.61)	67	1.29 (0.85, 1.95)
	IIIA	126	2.21 (1.52, 3.22)	118	2.06 (1.42, 2.99)
	IIIB	268	3.57 (2.56, 4.98)	208	2.72 (1.93, 3.82)
	IIIC	57	5.12 (3.39, 7.74)	39	3.37 (2.11, 5.37)
	IV	211	10.38 (6.86, 15.70)	123	6.74 (4.37, 10.30)
Age (y)	18-29	40	1.56 (1.10, 2.22)	32	1.74 (1.18, 2.56)
	30-39	155	1.19 (0.96, 1.47)	119	1.24 (0.98, 1.58)
	40-49	203	1	162	1
	50-59	185	1.03 (0.84, 1.27)	142	1.02 (0.81, 1.29)
	60-69	126	1.14 (0.90, 1.43)	96	1.12 (0.86, 1.45)
	70+	103	1.22 (0.94, 1.60)	68	1.03 (0.75, 1.41)
Tumour subtype*	ER+/PR+ HER2-	190	1	156	1
	ER+/PR+ HER2+	77	1.17 (0.89, 1.53)	58	1.03 (0.76, 1.39)
	ER- PR- HER2+	42	1.56 (1.11, 2.19)	30	1.40 (0.94, 2.09)
	ER- PR- HER2-	92	1.89 (1.47, 2.44)	76	1.91 (1.44, 2.53)
Treatment (at all stages)					
	Systemic therapy+sx†	308	1	289	1
	Systemic therapy, no sx†	282	2.16 (1.76, 2.65)	206	2.06 (1.65, 2.56)
	Sx†, no systemic therapy	37	1.45 (1.00, 2.10)	36	1.51 (1.03, 2.21)
	No treatment	185	2.11 (1.66, 2.67)	88	1.36 (1.02, 1.81)
Additional multiplicative treatment effect in women with metastatic disease					
	Systemic therapy, no sx†	-	0.76 (0.51, 1.13)	-	0.67 (0.43, 1.05)
	Sx†, no systemic therapy	-	0.30 (0.10, 0.90)	-	0.23 (0.07, 0.78)
	No treatment	-	1.84 (1.16, 2.90)	-	1.60 (0.82, 3.07)
HIV	Negative/NK	678	1	516	1
	Positive	134	1.39 (1.13, 1.70)	103	1.45 (1.15, 1.82)
Education	Tertiary	98	1	82	1
	Secondary	225	1.68 (1.32, 2.14)	173	1.57 (1.20, 2.06)
	Primary	336	1.71 (1.34, 2.19)	248	1.59 (1.20, 2.10)
	None	153	2.08 (1.56, 2.78)	116	2.13 (1.54, 2.95)
Group	Namibia, white	6	0.50 (0.22, 1.15)	6	0.56 (0.24, 1.30)
	Namibia, mixed race	9	1.23 (0.62, 2.45)	7	1.17 (0.53, 2.54)
	Namibia, black	140	1	117	1
	South Africa, mixed race	8	1.06 (0.51, 2.18)	7	1.25 (0.58, 2.71)
	South Africa, black	196	0.96 (0.76, 1.21)	148	1.04 (0.81, 1.35)
	Uganda	211	1.19 (0.82, 1.72)	168	1.20 (0.820 1.80)
	Zambia	72	1.15 (0.77, 1.71)	40	0.92 (0.60, 1.54)
	Nigeria	170	1.50 (1.01, 2.22)	126	1.66 (1.08, 2.56)

* A category for missing subtype was included (411 deaths to 3 years) to include women from Uganda, Nigeria and Zambia where subtypes were largely missing, thus survival gap apportionment to subtypes is not estimated in these countries. † sx = surgery. Systemic therapy = chemotherapy and/or endocrine therapy.

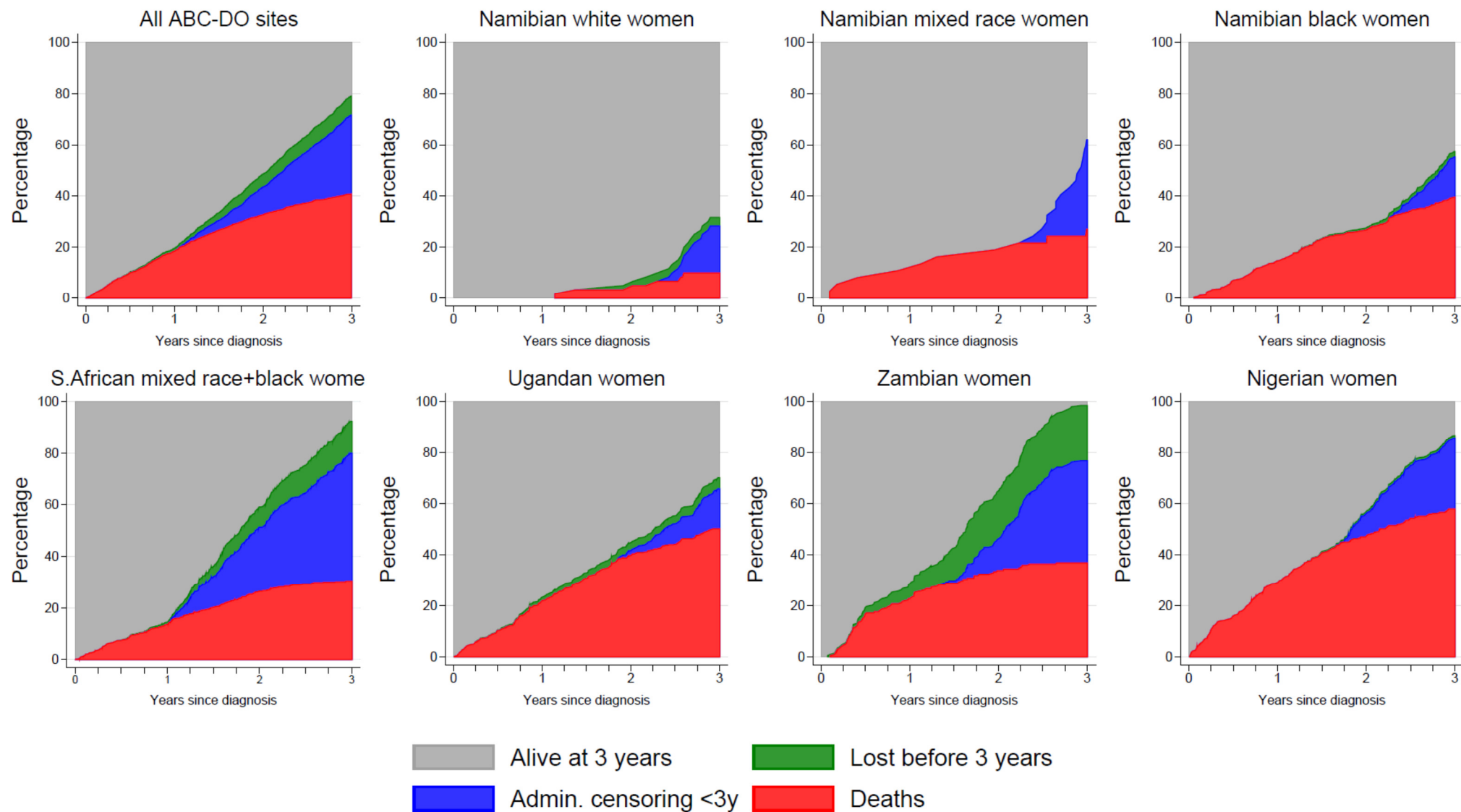
Supplementary Table 8: Three-year crude overall survival by group, observed and predicted upon shifting the stage distribution and thereafter upon accumulation of the elimination of survival disadvantages associated with lack of surgery + systemic therapy, social inequalities, HIV+, <30 y at diagnosis, and, in Southern Africa, non-ER+/PR+ HER2- tumour subtypes

	Namibia white	Namibia mixed race	S. Africa mixed race	Namibia black	S. Africa black	Uganda	Zambia	Nigeria public		Namibia white	Namibia mixed race	S. Africa mixed race	Namibia black	S. Africa black	Uganda	Zambia	Nigeria public
No. f women	60	35	36	369	635	421	197	309		60	33	35	346	586	377	160	266
3-year overall survival									3- year survival conditional on being alive at 6 months								
Current	88.5	69.8	69.4	58.0	60.7	44.8	43.3	38.4	88.1	76.4	67.7	62.2	63.9	49.5	59.5	43.6	
+ stage	89.8	72.4	76.1	66.6	66.2	54.2	52.3	50.1	89.5	76.4*	73.8	68.8	67.2	56.9	63.2	52.8	
+treatment	90.8	74.8	79.9	72.4	71.8	62.5	64.3	60.8	90.3	78.6	77.4	73.8	71.7	62.7	70.7	59.8	
+ education	92.9	79.2	80.8	76.6	73.9	67.1	68.4	65.9	92.3	82.1	78.4	77.6	73.9	67.1	73.8	64.3	
+HIV	92.9	79.7	81.4	77.6	75.7	68.1	69.7	66.0	92.3	82.5	79.2	78.6	75.9	68.3	75.0	64.5	
+age	93.0	79.9	82.0	77.9	75.8	68.8	70.5	66.4	92.4	82.7	80.1	79.1	76.1	69.2	75.8	64.9	
+ subtype	93.8	84.0	83.8	81.4	79.3	-	-	-	93.1	86.1	81.7	81.8	78.9	-	-	-	
Incremental change in 3-year survival percentage points due to change in individual factor																	
Current	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
+ stage	1.3	2.6	6.7	8.7	5.4	9.4	9.0	11.7	1.4	0.0	6.2	6.6	3.4	7.3	3.7	9.2	
+treatment	0.9	2.4	3.8	5.8	5.6	8.3	12.0	10.7	0.9	2.1	3.6	5.0	4.5	5.9	7.5	7.0	
+ education	2.2	4.4	0.9	4.2	2.1	4.6	4.1	5.1	2.0	3.5	1.0	3.8	2.2	4.4	3.1	4.5	
+HIV	0.0	0.5	0.6	0.9	1.8	0.9	1.3	0.1	0.0	0.4	0.8	1.0	2.0	1.1	1.2	0.2	
+age	0.0	0.2	0.6	0.4	0.1	0.7	0.8	0.4	0.1	0.3	0.9	0.5	0.2	0.9	0.8	0.5	
+ subtype	0.8	4.1	1.8	3.5	3.5	-	-	-	0.8	3.3	1.6	2.7	2.8	-	-	-	
Absolute percent change in 3-year survival, with cumulative effects of changes																	
Current	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
+ stage	1.3	2.6	6.7	8.7	5.4	9.4	9.0	11.7	1.4	0.0	6.2	6.6	3.4	7.3	3.7	9.2	
+treatment	2.2	5.0	10.4	14.4	11.1	17.6	21.0	22.4	2.2	2.1	9.7	11.6	7.8	13.2	11.2	16.2	
+ education	4.4	9.4	11.3	18.7	13.2	22.3	25.1	27.5	4.2	5.7	10.8	15.4	10.1	17.6	14.3	20.7	
+HIV	4.4	9.9	11.9	19.6	14.9	23.2	26.4	27.7	4.2	6.0	11.6	16.4	12.1	18.7	15.5	20.9	
+age	4.4	10.1	12.5	19.9	15.1	23.9	27.1	28.0	4.3	6.3	12.4	16.9	12.2	19.6	16.3	21.4	
+ subtype	5.2	14.1	14.4	23.4	18.5	-	-	-	5.0	9.6	14.0	19.6	15.1	-	-	-	
Predicted deaths at 3 years in 100 women																	
Current	11	30	31	42	39	55	57	62	12	24	32	38	36	50	41	56	
+ stage	10	28	24	33	34	46	48	50	11	24	26	31	33	43	37	47	
+treatment	9	25	20	28	28	38	36	39	10	21	23	26	28	37	29	40	
+ education	7	21	19	23	26	33	32	34	8	18	22	22	26	33	26	36	
+HIV	7	20	19	22	24	32	30	34	8	18	21	21	24	32	25	36	
+age	7	20	18	22	24	31	30	34	8	17	20	21	24	31	24	35	
+ subtype	6	16	16	19	21	-	-	-	7	14	18	18	21	-	-	-	

	% reduction in deaths with cumulative changes															
Current	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
+ stage	11	9	22	21	14	17	16	19	11	0	19	18	9	15	9	16
+treatment	19	17	34	34	28	32	37	36	19	9	30	31	22	26	28	29
+ education	38	31	37	44	34	40	44	45	35	24	33	41	28	35	35	37
+HIV	38	33	39	47	38	42	47	45	35	26	36	43	33	37	38	37
+age	39	33	41	47	38	43	48	45	36	27	38	45	34	39	40	38
+ subtype	46	47	47	56	47	-	-	-	42	41	43	52	42	-	-	-

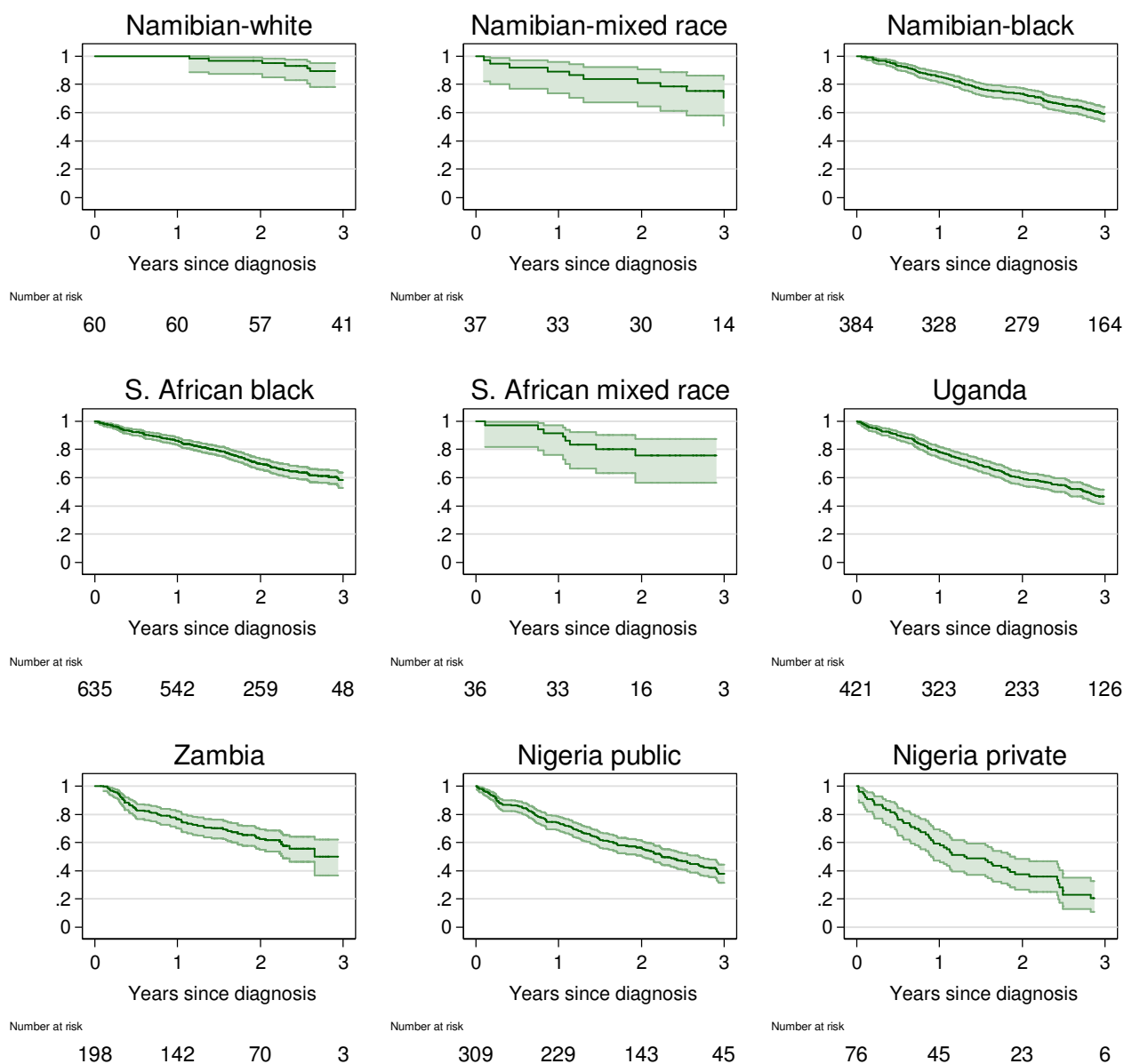
Small differences between estimates of crude survival (table 2) and the above 'current' 3-year survival arise because Table 2 is a crude Kaplan Meier estimate whereas Table 4 is a prediction based on women with complete data. *In the small group of mixed-race women in Namibia, the stage distribution was already better than the stage scenario consider, thus the observed distribution was not altered for the prediction.

Supplementary Figure 2: Follow-up status to 3 years post breast cancer diagnosis, ABC-DO entire cohort and by site-race group. Note that women identified as “lost before 3 years” are still being contacted, and continued contact attempts may result in an updated uncensored vital status in the future.



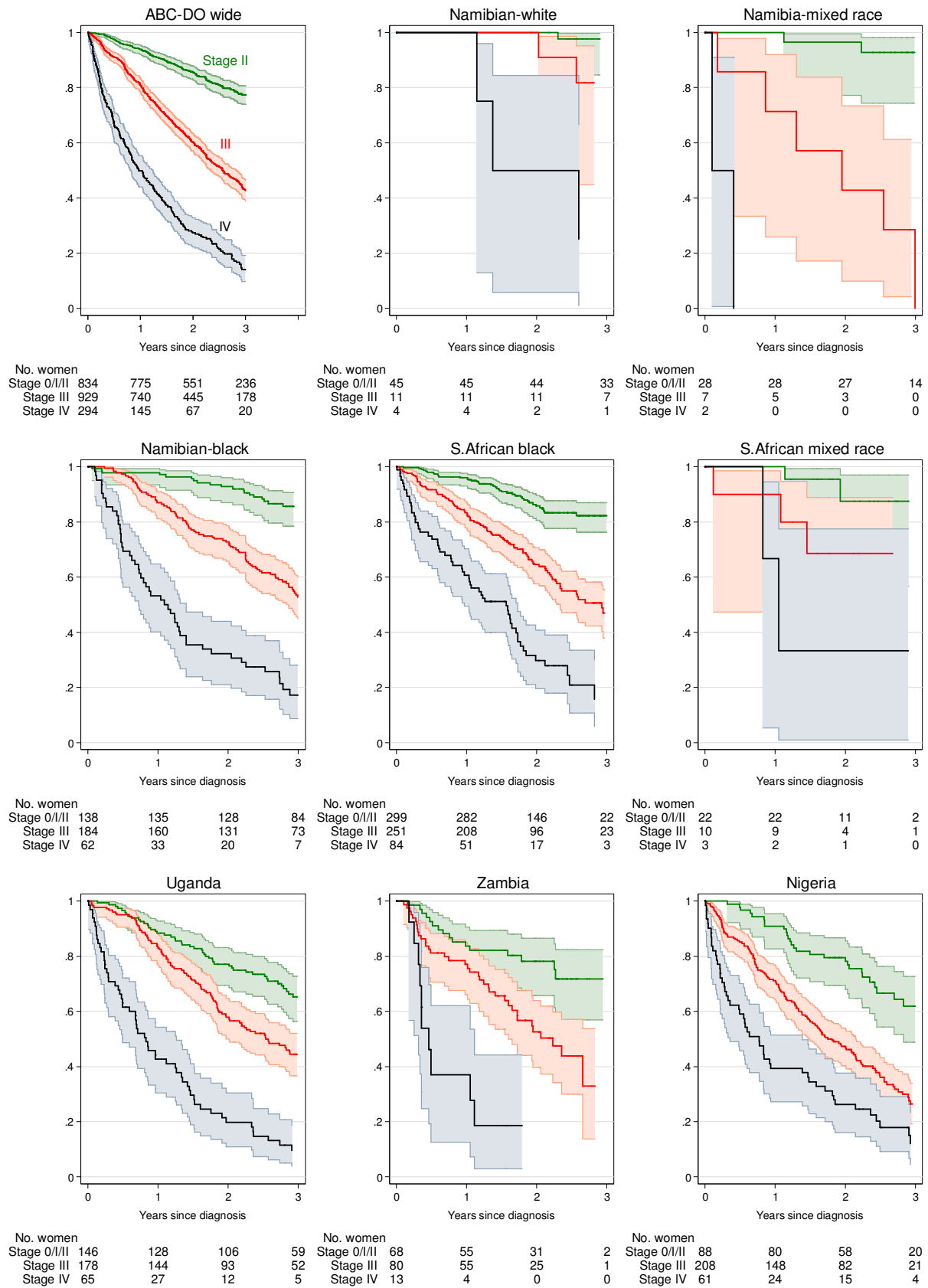
Supplementary Figure 3: Kaplan-Meier overall survival after breast cancer diagnosis, by site and race in the hospital-based ABC-DO cohort

Crude survival by site-race group



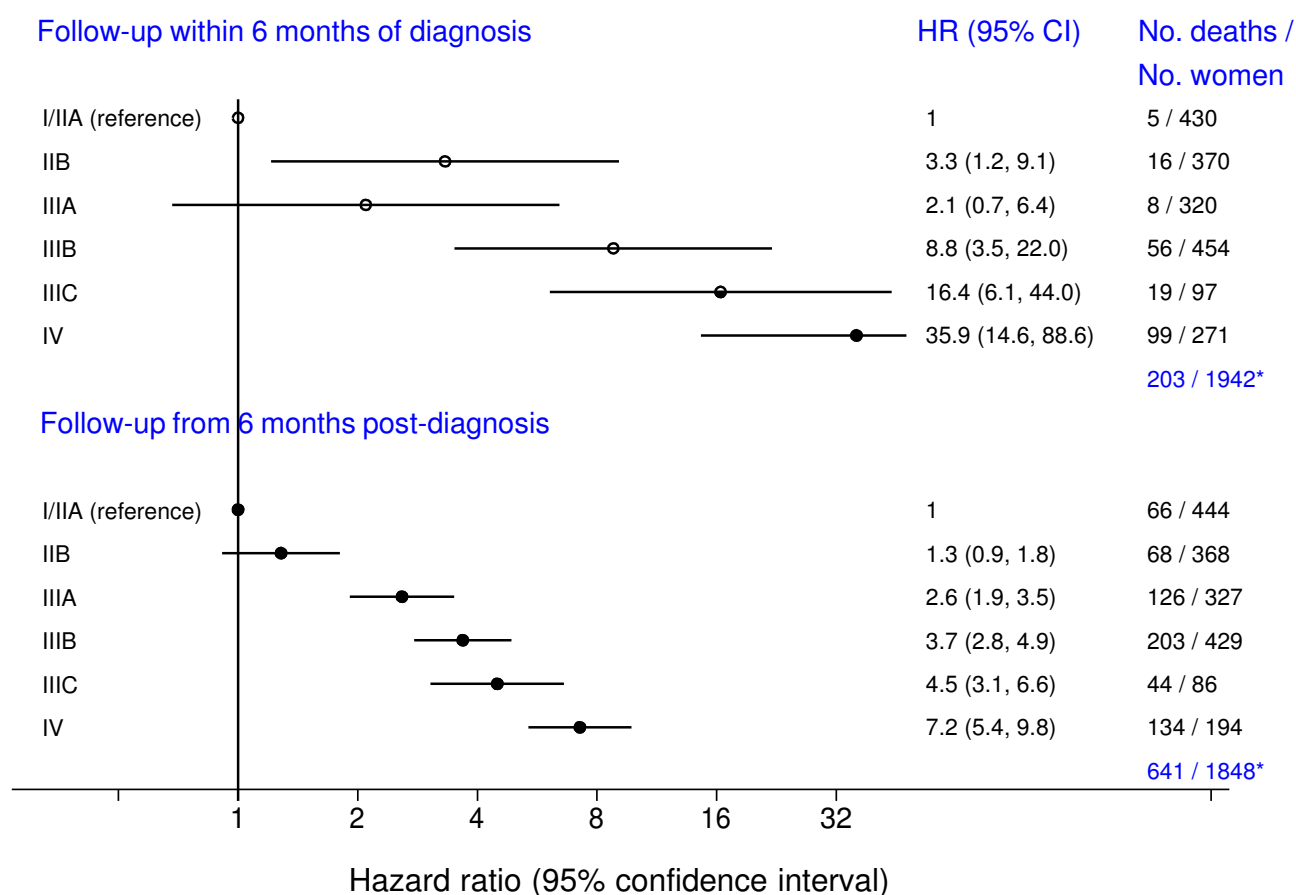
Supplementary Figure 4: Kaplan-Meier overall survival after breast cancer diagnosis for stage I/II, III and stage IV disease at diagnosis, by site and race in the hospital-based ABC-DO cohort

Crude survival by stage at diagnosis, overall and by site-race group



Subset	Log rank test p-value	Hazard ratio (95% CI) for Stage III v I/II	Hazard ratio (95% CI) for Stage IV v I/II
ABCD0 wide	p<0.0001	3.2 (2.7, 3.9)	8.4 (6.9, 10.3)
Namibia white	p<0.0001	8.2 (0.7, 90.4)	52.8 (5.5, 512)
Namibia mixed race	p<0.0001	20.6 (4.1, 105)	267 (16.7, 4266)
Namibia black	p<0.0001	4.0 (2.4, 6.5)	12.8 (7.5, 21.8)
S. African black	p<0.0001	3.3 (2.3, 4.8)	8.6 (5.7, 12.9)
S. African mixed race	0.0112	3.9 (0.6, 23.3)	12.7 (1.7, 92.9)
Uganda	p<0.0001	1.9 (1.3, 2.7)	6.3 (4.3, 9.4)
Zambia	p<0.0001	2.4 (1.3, 4.4)	8.4 (3.7, 19.1)
Nigeria	p<0.0001	2.8 (1.8, 4.2)	5.2 (3.3, 8.2)

Supplementary Figure 5: Effect of cancer stage on mortality



*Totals

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